APPROACH TO A PATIENT OF ANAEMIA

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Objectives

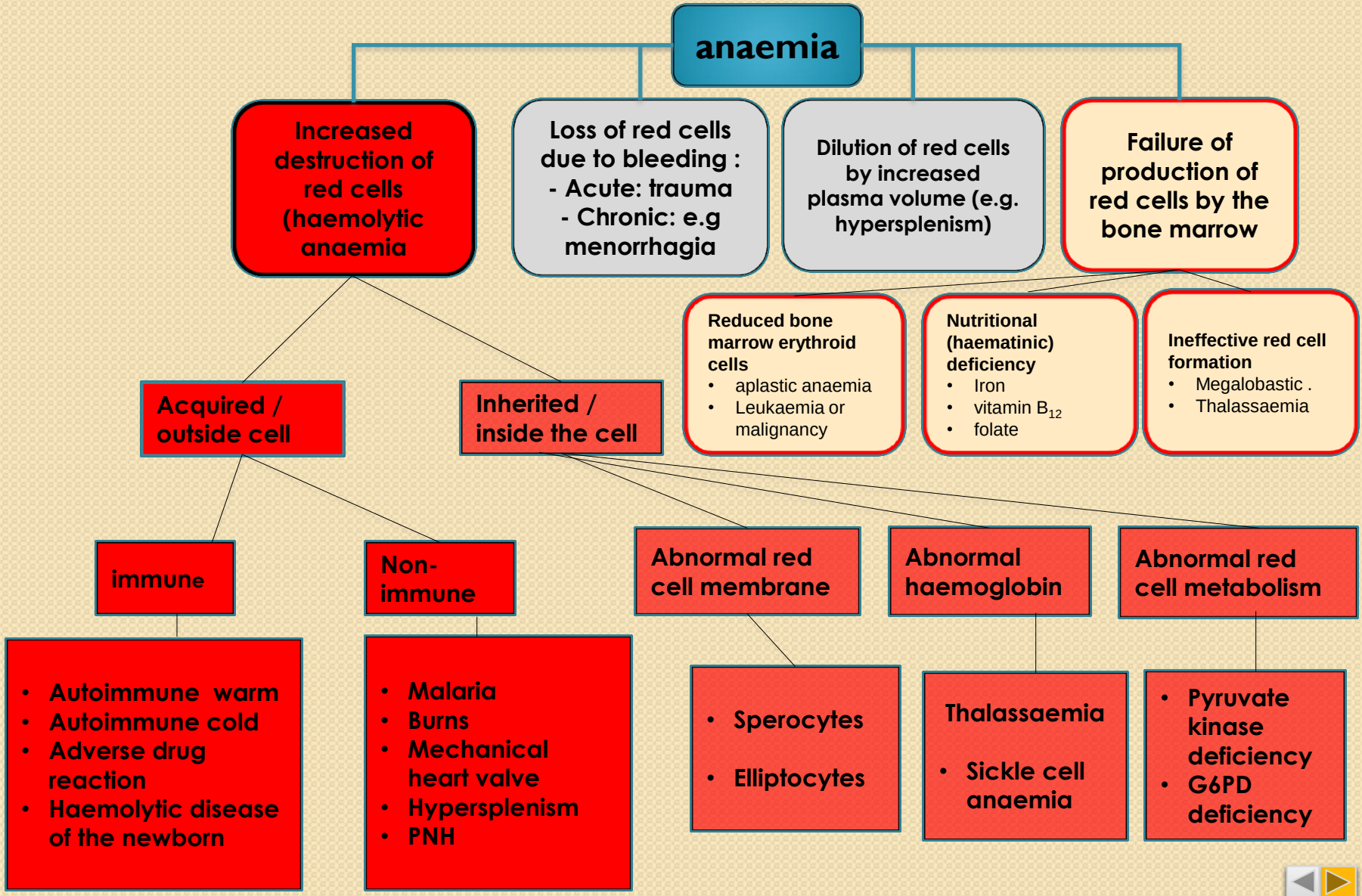
By the end of this lecture the student must be able to:

- Obtain pertinent history, physical and indicated laboratory studies
- Interpret studies for accurate differential diagnosis

KEY QUESTIONS

- *Is the patient really anaemic?*
- Hereditary / Acquired.
  (Acute or lifelong?)
- Compensated / Decompensated.
  (Acute anaemia / Chronic anaemia) & (Severity) .
- Medical condition associated with anemia?
- Is it deficiency anaemia ?
- Pancytopenia / Pure red cell aplasia?
- Which type in etiological classification?
  (↓ Production / ↑ Destruction / Loss)
- Which type in morphological classification.

Classification of anaemia based on pathology



Is the patient really anaemic? "Normal Range"

Variables:

- Volume status, age, gender, race, high altitude, pregnancy

WHAT IS ANEMIA?

Definition of Anemia

- Anemia is a decrease in the RBC count, Hgb and/or HCT values as compared to normal reference range for age and sex

(Also determined by alteration in plasma volume)

- ANEMIA IS NEVER NORMAL
- Men: HGB < 13.5 or HCT < 41%
- Women: HGB < 12.0 or HCT < 36%

Causes of Anemia

Kinetic Approach

- Decreased RBC production
- Increased RBC destruction
- Blood loss

Morphologic Approach

- Based on measurement of RBC size
  - Normocytic
  - Microcytic
  - Macrocytic

Causes of pancytopenia:

- Aplasia *(congenital/ acquired)*
- Leukaemia / solid tumours
- Megaloblastic
- Fibrosis
- PNH

Pure red cell aplasia

- Congenital
- Acquired *(viral/ autoimmune/ drug)*

Pancytopenia / Pure red cell aplasia?

Diagnostic approach to anemia

1. Review prior CBCs
2. Take comprehensive history and physical
3. Classify anemia by MCV
   - Microcytic (MCV <80 fL)
   - Normocytic (MCV 80-100 fL)
   - Macrocytic (MCV >100 fL)
     - Mild macrocytosis MCV 100-110 fL
     - Marked macrocytosis MCV >110 fL
4. Laboratory Evaluation
   - **CBC with RETICULOCYTE COUNT** (classification of proliferation)
   - **Review peripheral blood smear**
   - Order appropriate additional tests

History

Family history Spherocytosis Sickle cell anemia Thalassemia **Diet** Vegetarian **Drugs/Toxins** **Infection**	**Alcohol Abuse** Folate deficiency Liver disease **Malabsorption** B_{12} Folate Iron **Exposure** Lead Chemotherapy	**Peptic Ulcer** **Diverticulitis** **Colonic Polyps** **GI Malignancy** colorectal esophageal **Recent Surgery** **Travel**

Symptoms

Weakness Fatigue Difficulty in concentration Dizziness Headache Noise in ear Depression Chest pain Palpitations pale brittle nails Pica (clay, dirt, chalk, ice)	Cold intolerance soreness in the mouth Glossities Dysphagia Fever Petechiae, Ecchymoses Jaundice Diarrhea Constipation	Melena Hematuria Menorrhagia Hematoma Hematemesis Cessation of menstruation Loss of libido.

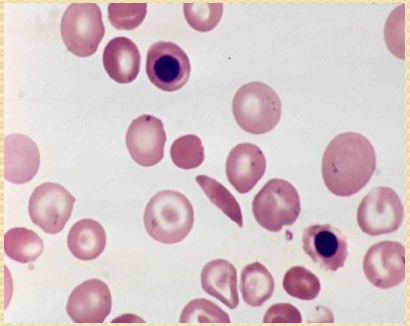
Physical Exam

Assess severity and find signs of organ or multisystem involvement.

Skin/ Mucosa Pallor, Mouth ulcer, Skin dryness, palmar creases, Thin/Brittle Spoon-shaped nails, Purpura **Angular Cheilitis** Iron Deficiency **Glossitis** B_{12} / Folate / Iron **Tachycardia**	**Bleeding,** **Occult blood,** **Jaundice** Liver Disease Hemolysis **Splenomegaly** Malignancy Infection Liver disease Chronic Hemolysis **Lymphadenopathy,** **Oedema**	**Neurologic** Paresthesias Ataxia Dementia **Gall stones** (hemolytic) **Dark urine** (hemolytic) **Bone deformity** (some haemolytic) **Leg ulcers** (some haemolytic).

Laboratory Evaluation

- CBC, *(Hb, RBCs count, Hct, MCV, MCH, RDW)*, to include TLC, WBC differential, platelet count, and reticulocyte count.
- Peripheral smear



- Iron Profile
  (Serum iron, TIBC, Ferritin, % Saturation)
- Folate/ B12 levels

WBC Count & Differential

- Leukopenia:
  - bone marrow suppression
  - Hypersplenism
  - deficiencies
- Leukocytosis:
  - Infection
  - Inflammation
  - malignancy

Useful tests in selected cases

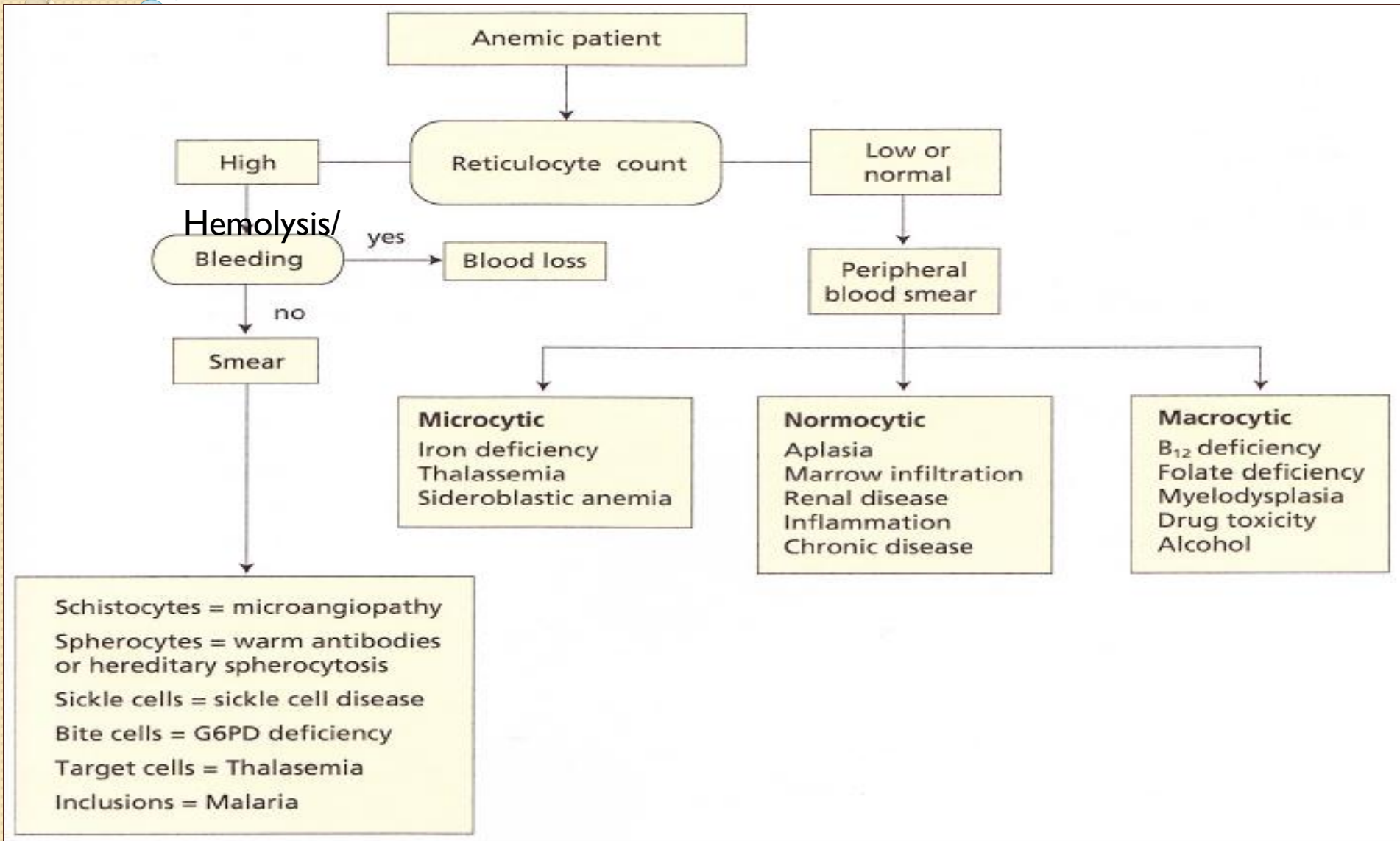
- Creatinine
- CRP/ESR
- ANA
- TSH
- Chronic hepatitis panel
- Homocysteine
- Methylmalonic acid
- SPEP

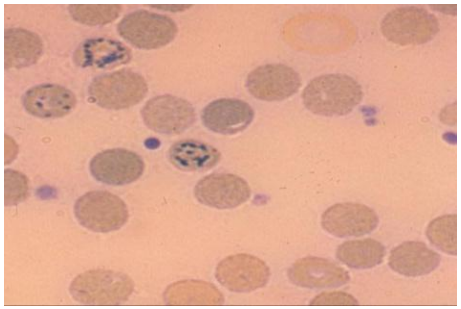
Indication of Bone Marrow Examination in Anaemic Patient !!!

- **Indications**:
  - Pancytopenia
  - Abnormal cells (blasts)

- **Diagnoses**:
  - Aplastic Anemia
  - Myelodysplasia
  - Malignancy
  - Myeloproliferative D

ALGORITHM FOR EVALUATION OF ANEMIA





ANEMIC PATIENT

Retic index

Hyper-regenerative

- **Hemolysis**
- **Blood loss**

Hypo-regenerative

Rule out ;

- Nutritional deficiency (iron, B-12, folate)
- Marrow dyscrasia (leukemia, myelodysplasia, aplastic anemia etc)
- Low EPO state (renal disease, inflammation, endocrinopathy, ? old age)

Retic Index:

> 2% = adequate response;

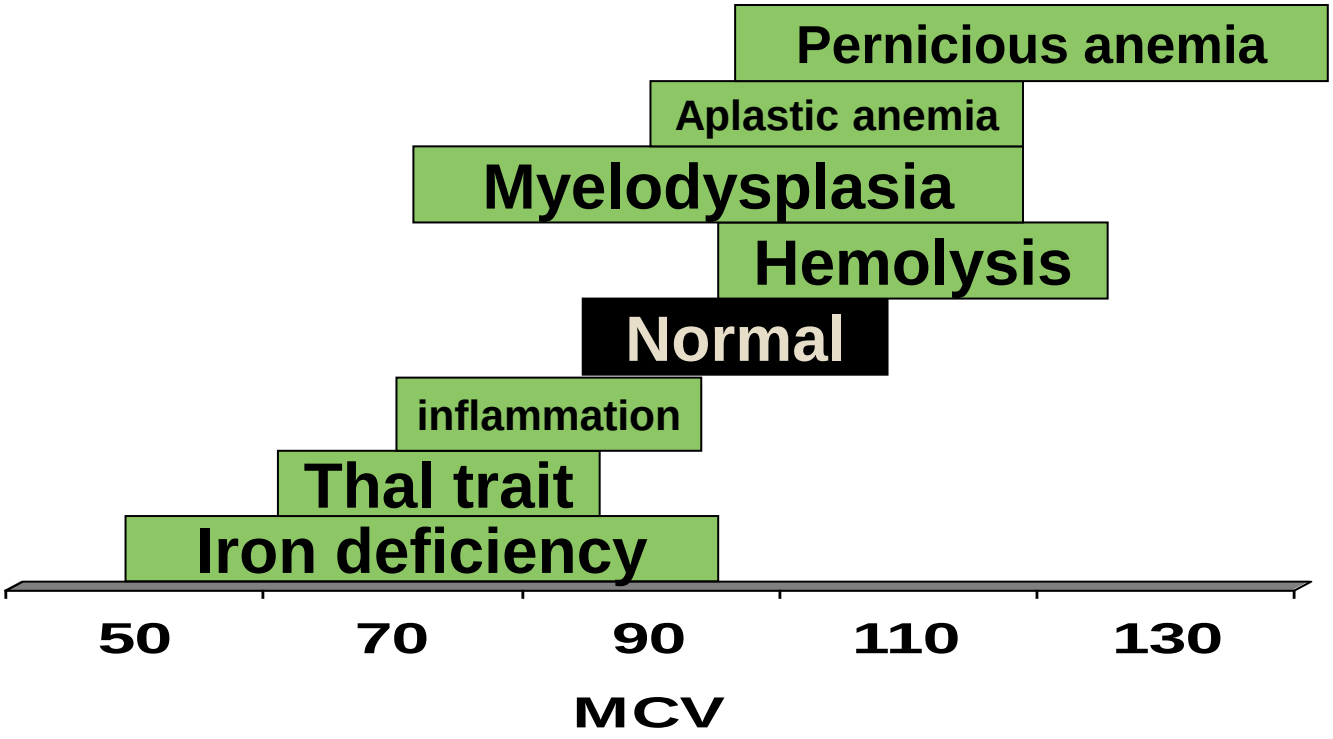
Reticulocyte Response

- Normal or low RI in the presence of anemia implies hyporegenerative state
- Very high RI (>4) suggests hemolysis/ blood loss.

Interpreting the MCV

The MCV reflects the average size of RBC

- Macrocytic (MCV >95)
- Microcytic (MCV <82)
- Normocytic



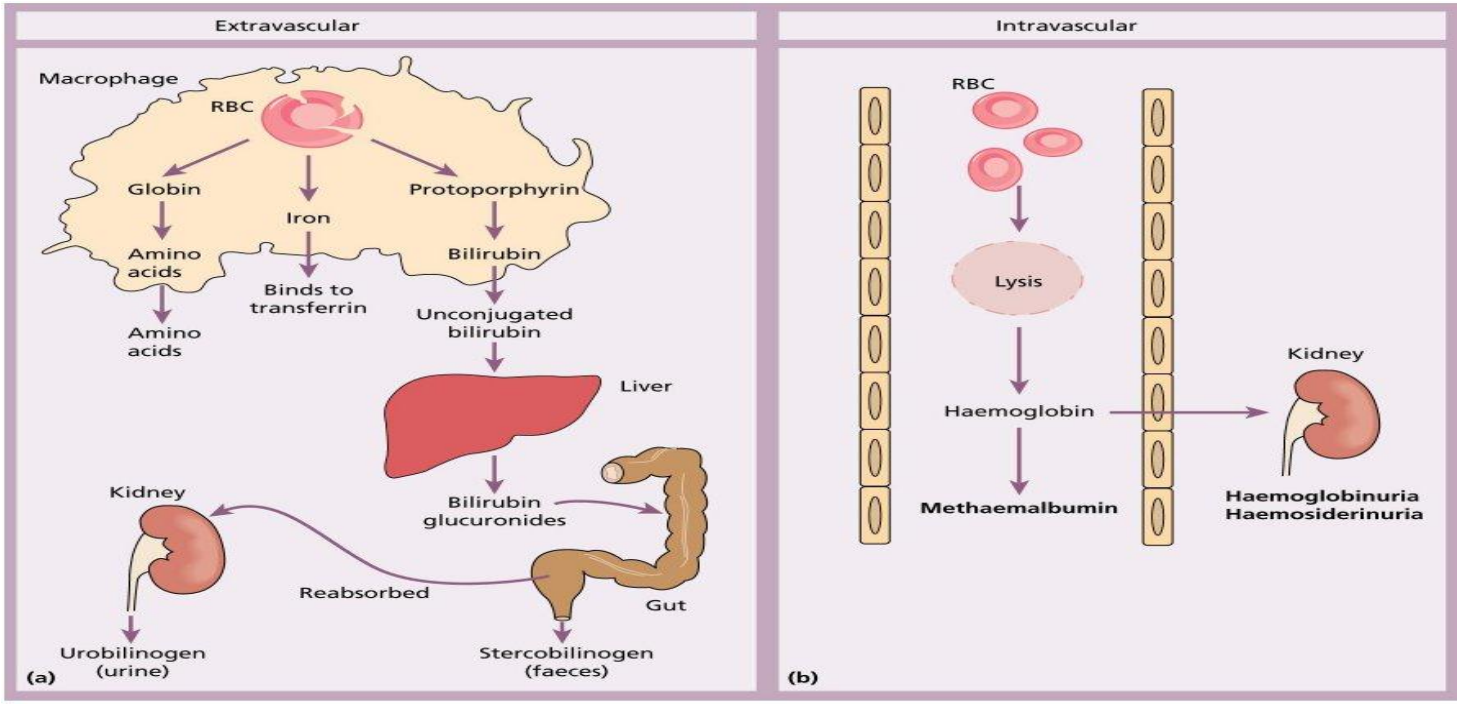
DIFFERENTIAL DIAGNOSIS GUIDED BY RETIC INDEX, MCV

- **Hyporegenerative**
  - Normocytic
  - Microcytic
  - Macrocytic
- **Hyperregenerative**

Hemolytic Anaemias;

Key Q.

- Hereditary/ Acquired ?
- Is the cause of hemolysis Extrinsic / Intrinsic?
- Intravascular/ extravascular ?
- Immune/ non immune



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Normocytic, Hypor-egenerative Anaemias

Marrow disorders

- Aplastic anemia
- Pure red cell aplasia
- Inherited anemia (Diamond-Blackfan)
- Myelophthisic state
- Myelodysplasia
- Leukemia and other heme malignancy

Low EPO state

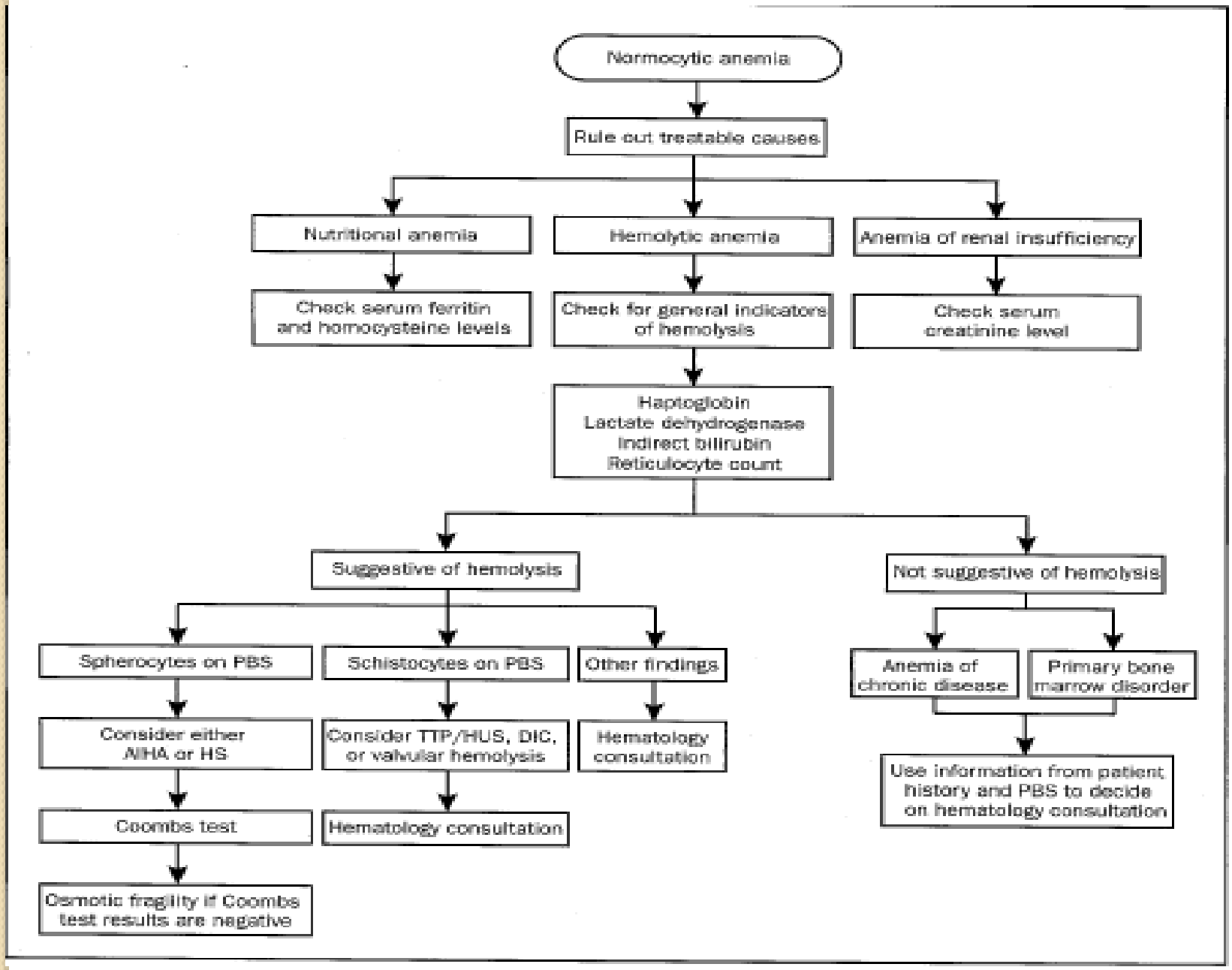
- Uremia, inflammation, endocrinopathy, HIV infection, etc
- Relatively common in elderly

Normocytic, Hyper-regenerative Anaemias

1- Blood loss

2- Hemolysis:

- **Congenital**:
  - Defect in the erythrocyte membrane *(Hereditary Spherocytosis)*
  - Defect in the erythrocyte metabolic enzyme *(G6PD Deficiency)*
  - Defect in hemoglobin structure or synthesis *(α - and β-Thalassemia & Sickle Cell disease)*
- **Acquired**:
  - Autoimmune hemolytic anemia *(WAIHA, Cold agglutinin disease)*
  - Microangiopathic hemolytic anemia *(TTP, DIC)*
  - Paroxysmal Nocturnal Hemoglobinuria
  - Infectious, chemical agents *(Malaria, arsinic, venom & toxin)*


Normocytic anemia
Rule out treatable causes
Nutritional anemia
Hemolytic anemia
Anemia of renal insufficiency
Check serum ferritin and homocysteine levels
Check for general indicators of hemolysis
Check serum creatinine level
Haptoglobin
Lactate dehydrogenase
Indirect bilirubin
Reticulocyte count
Suggestive of hemolysis
Not suggestive of hemolysis
Spherocytes on PBS
Schistocytes on PBS
Other findings
Anemia of chronic disease
Primary bone marrow disorder
Consider either AIHA or HS
Consider TTP/HUS, DIC, or valvular hemolysis
Hematology consultation
Use information from patient history and PBS to decide on hematology consultation
Coombs test
Hematology consultation
Osmotic fragility if Coombs test results are negative

Evaluation for Hemolysis

- *Rapid fall in HGB*
- *Reticulocytosis*
- *Abnormally shaped RBC*

- **Measure:**

  - **Non specific indicator for hemolysis:** **(***LDH, Indirect bilirubin).*
  - **Indicators of intravascular hemolysis:** *(haptoglobin, urine hemosiderin, plasma or urine hemoglobin)*
  - **Other:** *Direct Coombs test (IgG / C3), Hgb electrophoresis, RBCs enzyme levels, G6PD, osmotic fragility, PNH testing* .. etc

Microcytic Anaemias

Microcytosis implies defective hemoglobin production

- **Iron deficiency (R/O GI bleeding!)**
- **Thalassemia**
- **Inflammation**
- **Sideroblastic anemia (myelodysplasia, lead poisoning etc)**

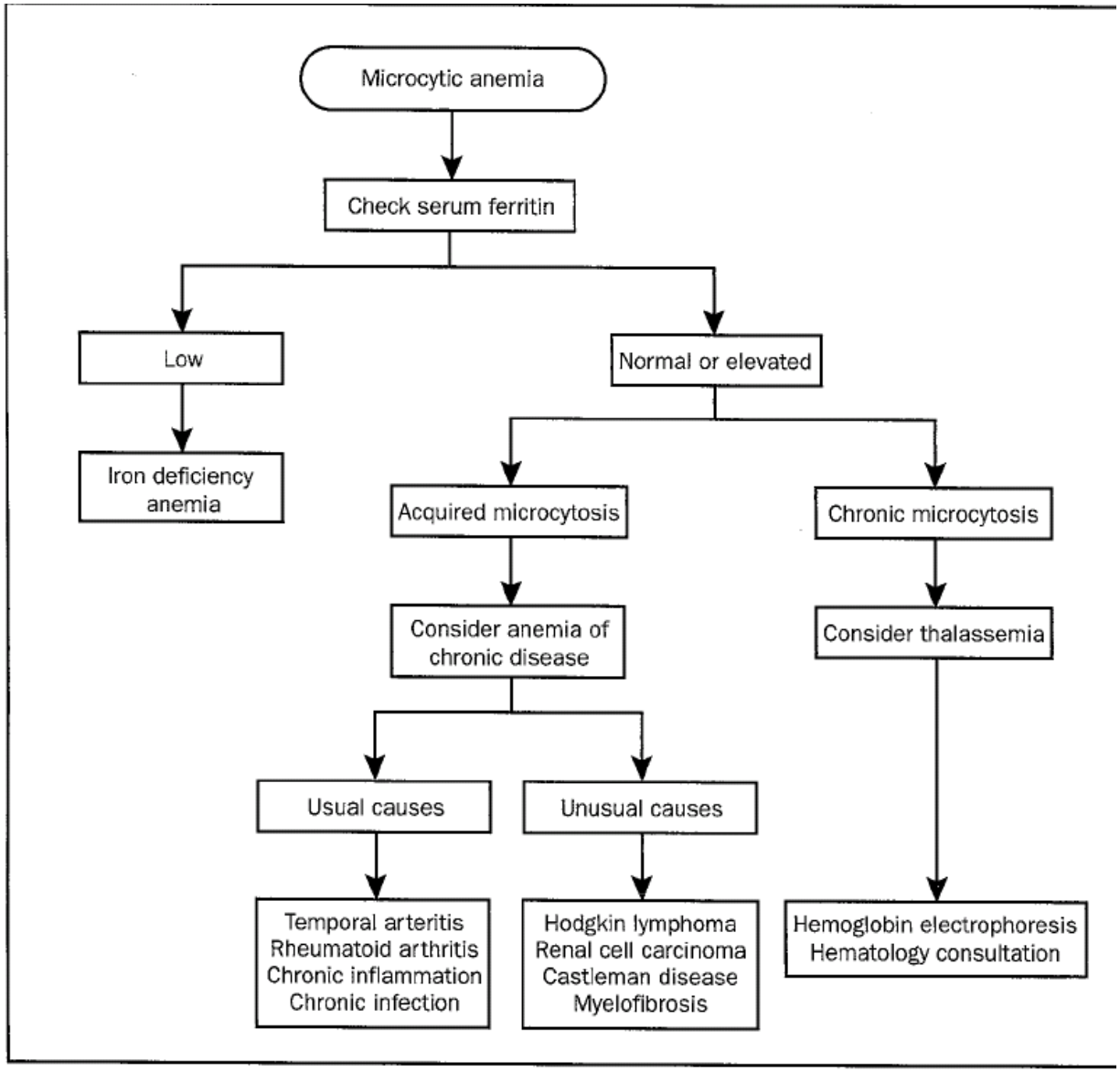


FIGURE 1. Diagnostic algorithm for microcytic anemia.

Laboratory assessment of microcytic anemia :

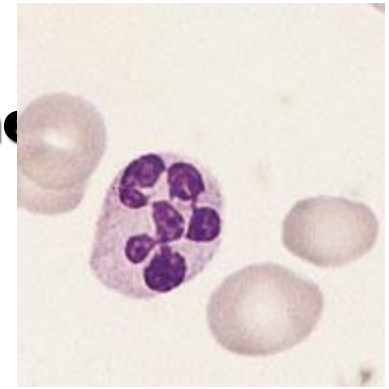
Test	Fe Deficiency	Anemia of inflammation	Thalasaemia
Ferritin	Low*	NL/high	NL
Serum Fe	Low	Low	NL
TIBC	High	NL/low*	NL
% Sat	Low	Low	NL
Retic index	NL/low	NL/low	NL/high

***best discriminators of Fe defic vs anemia of inflammation**

Macrocytic Anaemias

Megaloblastic:

- B12/folate deficiency
- Myelodysplastic syndrome
- Drug-induced



Non-megaloblastic:

- Liver disease
- Alcohol
- Hypothyroidism
- Reticulocytosis

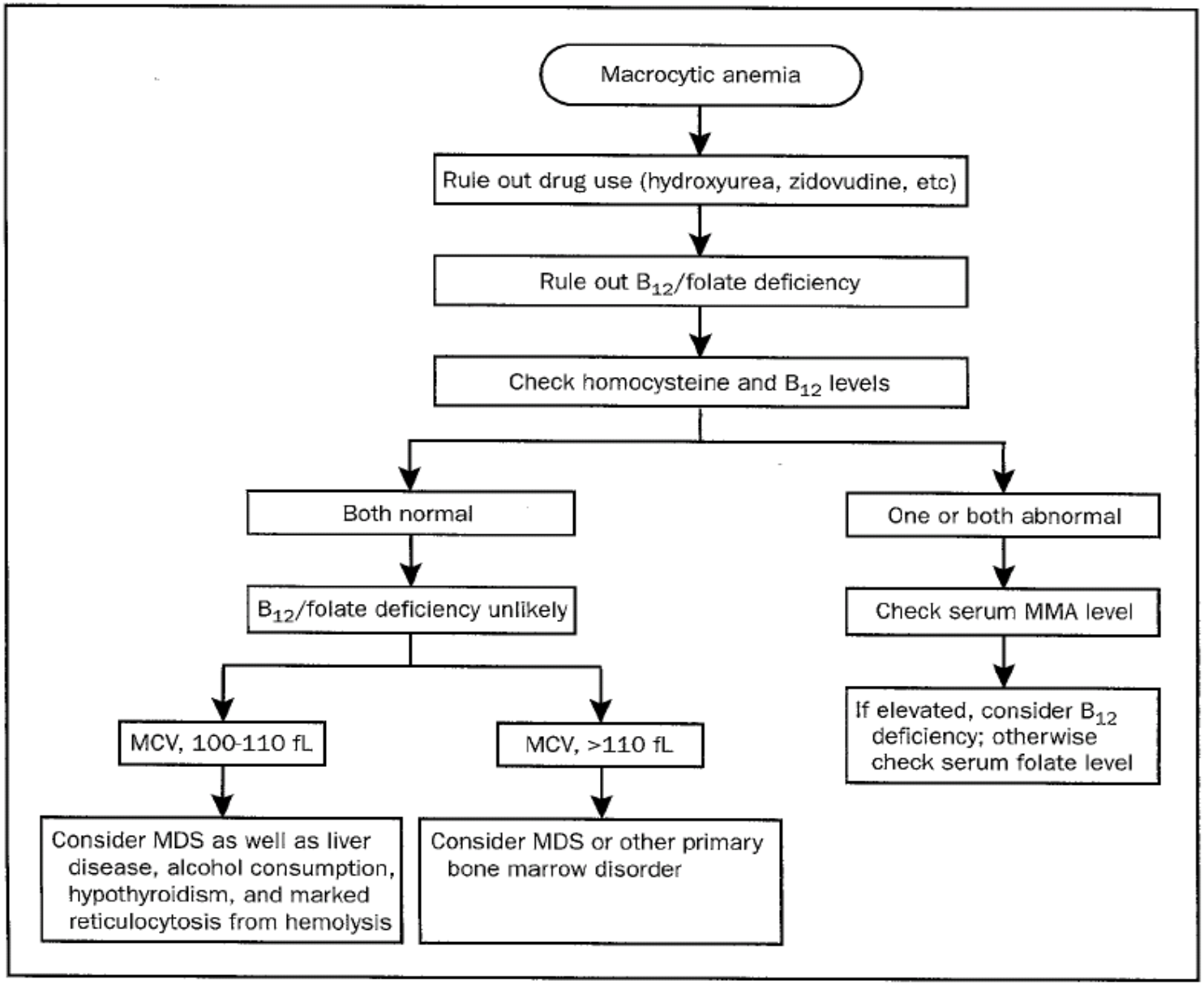


FIGURE 3. Diagnostic algorithm for macrocytic anemia. MCV = mean corpuscular volume; MDS = myelodysplastic syndrome; MMA = methylmalonic acid.

B-12/Folate deficiency

- **Therapeutic trial reasonable if blood level of vitamin borderline**
- **In equivocal cases consider confirmatory tests:**

TEST	DEFICIENCY
Methymalonate	B-12
Homocysteine	B-12 or folate